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EXAMINER

CRANE, L

ART UNIT

PAPER NUMBER

1623

DATE MAILED: 04/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.

09/192,167

Applicant(s)

Meade et al.

Examiner

L. E. Crane

Group Art Unit

1623

--The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address--

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ----3---- MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 6/17/99 (IDS) and 02/07/00 (Amdt A)-----

☒ This action is **FINAL**.

- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 2-14----- is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 2-14----- is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

☒ Claim 1 has been cancelled.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
 - ☐ received in Application No. (Series Code/Serial Number) _____.
 - ☐ received in this national stage application from the International Bureau (PCT Rule 1.7.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). ----6---- ☐ Interview Summary, PTO-413
- ☒ Notice of Reference(s) Cited, PTO-892 ☐ Notice of Informal Patent Application, PTO-152
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948 ☐ Other _____

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The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group 1600, Art Unit 1623.

- 5 Claim **1** has been cancelled and new claims **7-14** have been added as per the preliminary amendments filed February 7, 2000.

Claims **2-14** remain in the case.

- 10 Note to applicant (repeated one time): In each of the claims applicant is encouraged to define the new chemical reactants, particularly the newly modified nucleoside reactants and products, with complete chemical structures.

- 15 Claims **2-14** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- 20 In claim **7** the term "comprising" (first and third occurrences only) is incorrect in the instant claim because said term implies that the chemical structure of the compound being claimed contains additional structural component(s) not defined in the claim. Applicant is respectfully requested to substitute narrow language such as -- consisting of -- or the like for the noted term. The same problem reoccurs in claims **2 and 3**.

Applicant's arguments filed February 7, 2000 have been fully considered but they are not persuasive.

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Applicant is respectfully requested to note that without chemical formulas to define what the functional language is intended to define within the claims, applicant is unlikely to meet the minimum requirements of the statute.

5 In claim 7, lines 2-5, the terms "an anhydro-nucleoside", "an electron transport moiety", and "an activated anhydro-nucleoside" are generic terms with many possible structural meanings one, some or all of which may or may not be read into the instant claims in view of the total absence of adequate definition of the metes and
10 bounds intended to accompany said terms. For example, with 2-oxo-pyrimidine nucleosides (i.e. uridines and cytidines) there are at least 6 possible different anhydro-forms (2'-O², 3'-O², 5'-O², 2'-C⁶; 3'-C⁶ and 5'-C⁶). It is unclear which of these are intended and which are not by reading the instant claim. Also, the term "electron
15 transport moiety" reads on a copper wire and also reads on a functional group which is capable of gaining or losing electrons, e.g. the bio-oxidant NAD⁺ (gains electrons) and its bio-reductant pair NADH (loses electrons) may be modified with linkers to be substituents at the 2'-position of a 2'-deoxy-2'-amino nucleoside.
20 Clearly, neither of these possibilities were contemplated by applicant and are therefore not properly within the metes and bounds of the instant claim. More carefully drafted claims will insure that these alternatives are excluded from within the metes and bounds of applicant's claim.

25 Applicant's arguments with respect to claim(s) 1-6 have been considered but are moot in view of the new grounds of rejection.

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5 In claim 7, lines 6-8, the terms "cyclization agent" and "cyclized intermediate" are relatively meaningless unless the details of the chemical reaction being alluded to are provided, thereby rendering this portion of the instant claim lacking in adequately defined metes and bounds.

Applicant's arguments with respect to claim(s) 1-6 have been considered but are moot in view of the new grounds of rejection.

10 Applicant's complete reliance on functional terminology is the root of the problem. It is presently impossible for any practitioner to determine which functional groups are interacting with "an activation agent" when only one starting material functionality is partially defined. Similarly the definitions of the chemical compounds included within the metes and bounds of the terms "cyclization agent" and "cyclized intermediate" remain unclear. Examiner does
15 not know how to overcome this problem without resort to structural formulas. The use of this kind of terminology also renders searching for all of the prior art encompassed by claims 2-10 practically impossible.

20 In claim 2, adding a phosphoramidite moiety to a nucleoside is possible, but where such a group is being added in this case remains unclear because of the lack of clarity found in claims 7 and 2.

Applicant's arguments filed February 7, 2000 have been fully considered but they are not persuasive.

25 Applicant is respectfully requested to make much more specific what chemical structures are being referred to. Reliance on entirely

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functional terminology fails to "... particularly point out ..." the metes and bounds of the instant claimed subject matter.

5 In claim 3, adding a phosphoramidite-derivatized nucleoside to the terminus of a "growing" nucleic acid appears to make reference to the Caruthers process of nucleic acid synthesis, but remains indefinite for failure to specify the chemical structural variables which define the "phosphoramidite modified nucleoside."

Applicant's arguments filed February 7, 2000 have been fully considered but they are not persuasive.

10 Applicant is respectfully requested to amend the instant claim to "... particularly point out and distinctly claim ..." what applicant is making reference to. Because applicant has not done this, the instant rejection has been maintained.

15 In claim 5, the term "nucleoside analog" is indefinite because applicant has not provided adequate guidance within the instant claim to permit the ordinary practitioner to determine which compounds qualify as a "nucleoside analog" and which do not (an indefinite metes and bounds problem).

20 Applicant's arguments filed February 7, 2000 have been fully considered but they are not persuasive.

Applicant quotes the instant disclosure wherein the noted term is included. However, applicant is respectfully requested to note that the definition found in the disclosure does not solve the problem because the quoted definition is itself indefinite, i.e. the noted

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definition fails to define the noted term in other than functional terms and therefore fails to adequately limit the metes and bounds thereof.

5 In claim 6, the term "carbonyldimidazole" is misspelled. Did applicant intend the term to be spelled -- carbonyldiimidazole -- (emphasis added)?

Applicant's arguments filed February 7, 2000 have been fully considered but they are not persuasive.

10 Applicant's partial correction is noted. Applicant is respectfully requested to note that this chemical name when correctly spelled contains a double "i"; see underlining.

15 Claim 5 is objected to under 35 C.F.R. §1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

20 In claim 5, the term "nucleoside analog" is not a term usually thought to be encompassed by the term "nucleoside", thereby rendering the instant claim lacking in proper antecedent basis. Applicant may introduce by amendment -- further comprising -- language to effectively address this problem or take other appropriate action.

Applicant's arguments filed February 7, 2000 have been fully considered but they are not persuasive.

25 Applicant is respectfully requested to note that the term "nucleoside" does not include within its scope the instant noted term

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"nucleoside analog." Attempts by applicant to justify alteration of the well recognized meanings of these terms is not found to be either appropriate or acceptable. For these reasons, the instant rejection has been maintained.

5 In claim 8, the term "transition metal complexes" refers to compounds, not substituent moieties. Said language is also entirely functional so examiner is unable to know what particular complex or complexes applicant is referring to or how said complex or complexes is/are modified for attachment to the resultant product. Without this
10 information, a truly competent literature search to find the relevant prior art is effectively impossible.

Applicant's arguments with respect to claim(s) 1-6 have been considered but are moot in view of the new grounds of rejection.

15 In claim 9, the term "wherein said electron transfer moieties are selected from the group consisting of ruthenium, rhenium, osmium, platinum, cobalt and iron" is technically incorrect and incomplete because the structures of the "electron transfer moieties" must include other components than a metal or a metal ion. Applicant has therefore incompletely defined the "electron transfer moieties" by
20 failing to note in the claim all of the structural features intended to be included.

Applicant's arguments with respect to claim(s) 1-6 have been considered but are moot in view of the new grounds of rejection.

25 Claim 10 contains nearly all of the same problems defined above for claim 7. The term "a covalently attached polydentate ligand" only hints at the structure of the intended product. Also said term is

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inconsistent with other terms in dependent claims **13 and 14** including "ferrocene" (not a substituent but a compound which includes an Fe^{+2} ion coordinate-covalently bonded to two cyclopentadienyl anions) and "metallocene" (a name for the genus of organometallic compounds which includes ferrocene). As a
5 consequence of these technical errors, claims **13 and 14** both lack proper antecedent basis in claim **10**.

Applicant's arguments with respect to claim(s) **1-6** have been considered but are moot in view of the new grounds of rejection.

10 In claim **11**, the term "polydentate ligand" does not specify and therefore does not include any coordinate-covalently-bonded metal atom or ion. Therefore, applicant appears to err when equating the noted term with the term "an organometallic ligand." The term "an organometallic ligand." appears to be either internally inconsistent (a
15 ligand which contains metal atoms/ions within its structural backbone?) or said term fails to further limit the subject matter of claim **10** (e.g. EDTA is a "polydentate ligand" capable of forming complexes with metal ions (Zn^{+2} , Fe^{+3} , etc.) wherein the resultant complexes are "organometallic" compounds).

20 Applicant's arguments with respect to claim(s) **1-6** have been considered but are moot in view of the new grounds of rejection.

In claim **12**, the term "a organometallic ligand" contains a grammatical error. Did applicant intend the term to read -- an organometallic ligand--?

25 Applicant's arguments with respect to claim(s) **1-6** have been considered but are moot in view of the new grounds of rejection.

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Claims 2-14 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In claims 2-14, the chemical reactants are described using generic terms only, thereby encompassing a substantial area of subject matter for which applicant has failed to provide adequate enabling support within the instant disclosure. Specifically terms such as "anhydro-nucleoside" (claim 1), and "nucleoside analog" (claim 5) is directed to a vast array of chemical structures while applicant's specification only discloses a limited number of specific embodiments, leaving the ordinary practitioner the unreasonable burden of determining which claimed embodiments are actually operative and which are not (undue experimentation).

Applicant's arguments filed February 7, 2000 have been fully considered but they are not persuasive.

Applicant has cited judicial guidance to support the view that "... an inventor need not ... explain every detail" Applicant the argues that "anhydronucleoside" and "nucleoside analog" are art recognized terms. Examiner agrees that the noted terms are used in the art, but notes as well that the terms are generic, i.e. they do not have well defined metes and bounds. Applicant is applying for a property right and it is examiner's duty to insure that the grant of such rights is made in a manner which meets the statutory requirements of 35 U.S.C. §112, first paragraph and second paragraph. Since applicant is not submitting a review article to a

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5 scholarly journal or as a book chapter, the standard of review is as prescribed in the statute. Applicant is encouraged to use the instant specific embodiments (working examples) to devise claims which have a much more limited scope ("make and/or use" is the standard) and a much more precisely defined metes and bounds ("particularly point out and distinctly claim" is the standard).

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

10 "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall
15 not be negated by the manner in which the invention was made."

Claims 10-12 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nexstar '102 (PTO-892 ref. L).

20 The instant claims are directed to a process for making labelled nucleosides from anhydro-nucleosides wherein the label is a polydentate ligand.

25 The Nexstar '102 reference at page 62, claim 14, discloses two 2'-substituents (the last two at line ~10) which contain 7 and 3 oxygens, respectively, which substituents have the potential to act as ligands, thereby rendering same "polydentate ligands." In view of their synthesis via ring opening of the appropriate anhydronucleoside by an amino/amido nitrogen, the disclosed method of making these products is deemed to meet all of the limitations (implied and specified) of the instant claims.

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The disclosure in the prior art of methods of making compounds which read on the claimed method of making are deemed to render said method lacking in patentable distinction.

5 Therefore, the instant claimed process for making labelled nucleosides wherein the label is a polydentate ligand from anhydro-nucleosides would have been obvious to one of ordinary skill in the art having the above cited reference before him at the time the invention was made.

10 Applicant's arguments with respect to claim(s) 1-6 have been considered but are moot in view of the new grounds of rejection.

Claims 2-7 are rejected under 35 U.S.C. §103(a) as being unpatentable over Nexstar '102 (PTO-892 ref. L).

15 The instant claims are directed to a process for making labelled nucleosides from anhydro-nucleosides wherein the label is an "electron transfer moiety," for making the phosphoramidites thereof, and for making standard or modified oligonucleotides or polynucleotides therefrom via phosphoramidite coupling.

20 The Nexstar '102 reference discloses processes for making labelled nucleosides from anhydro-nucleosides, for making the phosphoramidites thereof, and for making standard or modified oligonucleotides or polynucleotides therefrom via phosphoramidite coupling. Applicant is referred to pages 17, 21, 23, 26, 3140, 49, 50 and 53, and claim 1, at p. 59, lines 10-11, and claims 5, 20, 22 and 25 wherein the last three claims disclose the nucleoside starting material, disclose the phosphoramidite analogues of the

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nucleoside, and imply the use of said phosphoramidites to make oligonucleotides incorporating the modified nucleosides by claiming compounds which could be the product of a phosphoramidite oligonucleotidesynthesis.

5 Teachings of the prior art which disclose in detail subject matter which reads on the invention as claimed is deemed to render the instant claims lacking in patentable distinction in view of the noted prior art.

10 Therefore, the instant claimed process for making labelled nucleosides from anhydro-nucleosides, for making the phosphoramidites thereof, and for making standard or modified oligonucleotides or polynucleotides therefrom via phosphoramidite coupling, would have been obvious to one of ordinary skill in the art having the above cited reference before him at the time the
15 invention was made.

Applicant's arguments with respect to claim(s) 1-6 have been considered but are moot in view of the new grounds of rejection.

20 Claims **8-9 and 13-14** are objected to as being dependent on a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and if rewritten or amended to overcome the rejection(s) under 35 U.S.C. §112 set forth in this Office Action.

25 Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

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A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS
5 FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY
10 EXTENSION FEE PURSUANT TO 37 C.F.R. §1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Papers related to this application may be submitted to Group
15 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone numbers for the FAX machines operated by Group 1600 are **(703) 308-4556** and **703-305-3592**.

20 Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **703-308-4639**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

25 If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor can be reached at (703)-308-1235.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is 703-**308-1235**.

5 LECrane:lec
04/17/00



PAUL J. KILLOS
PRIMARY EXAMINER

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